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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/910,958	07/24/2001	Brian S. Hooker	059440-0138	3645

7590

01/16/2003

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EXAMINER

BAUM, STUART F

ART UNIT

PAPER NUMBER

1638

DATE MAILED: 01/16/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/910,958

Applicant(s)

HOOKER ET AL.

Examiner

Stuart F. Baum

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED. (35 U.S.C. § 133)
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on 01 November 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☐ Claim(s) 1-44 is/are pending in the application.
- 4a) Of the above claim(s) 1-15, 20-28 and 36-44 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☐ Claim(s) 16-19 and 29-35 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on with application is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 6, 10
- 4) ☐ Interview Summary (PTO-413) Paper No(s): _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

1. Claims 1-44 are pending.

Applicant's election with traverse of Group II (F), claims 16-44 with those drawn to a light inducible promoter, in Paper No. 9 is acknowledged. The traversal is on the ground(s) that it would not require additional searches or otherwise place a serious burden on the PTO to search all claims. This is not found persuasive because while the search of the prior art for one group may overlap with that of another, they are not co-extensive of each other and thus would be a burden on the Office.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-15, 20-28, and 36-44 are withdrawn from considerations as being drawn to a non-elected invention.

Claims 16-19, and 29-35 are examined in the present office action.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 16-19 and 29-35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 16, the metes and bounds of "optimal expression" have not been defined. All subsequent recitations of "optimal expression" are also rejected.

In claim 16, the metes and bounds of "defined environmental conditions of CEA" have not been defined. All subsequent recitations of "defined environmental conditions of CEA" are also rejected.

In claim 29, the recitation "a plant system" has not been defined. It is unclear what components constitute "a plant system".

In claim 29, the metes and bounds of "a large amount" have not been defined. It is unclear how "a large amount" can be objectively measured by those skilled in the art. All subsequent recitations of "a large amount" are also rejected.

In claim 29, the metes and bounds of "rapidly propagated" have not been defined. It is unclear how "rapidly propagated" can be objectively measured by those skilled in the art.

In claim 29, the recitation "soluble protein extracts" has not been defined. It is unclear in what solvent or solution the protein extract would be soluble.

In claim 29, the recitation "increased" is a relative term and requires a comparative basis.

In claim 29, the metes and bounds of "other damage to heterologous protein targets" have not been defined. It is unclear what other process(es) would constitute "other damage".

In claim 29, the metes and bounds of "an extract" have not been defined. It is unclear what constitutes "an extract". An extract can be a solution composed of any solvent using any type of plant material, either shoots, roots, leaves or flowers.

In claims 30-35, it is unclear what process(es) or step(s) are encompassed by "is selected".

In claim 30, the metes and bounds of "about" have not been defined. All subsequent recitations of "about" are also rejected.

In claim 31, the recitation "greens" has not been defined. Is Applicant only referring to leaves, or are stems and flower organs included?

Scope of Enablement

3. Claims 16-19 and 29-35 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for producing a heterologous protein in a transformed plant does not reasonably provide enablement for a method for producing a heterologous protein in large amounts as recited in the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claimed invention is not supported by an enabling disclosure taking into account the *In re Wands* factors (858F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988)). *In re Wands* lists a number of factors for determining whether or not undue experimentation would be required by one skilled in the art to make and/or use the invention. These factors are: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples of the invention, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claim.

The Applicants have only exemplified the above mentioned constructs transformed into potato or the GUS gene transformed into various *Brassica* species. Applicants have not exemplified all heterologous encoding nucleic acids or even a sample population of a particular type of heterologous encoding nucleic acids. Applicants are proposing a method to overexpress

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proteins for the purpose of extracting or harvesting said proteins from the plant and has claimed large quantities of proteins to be harvested from said plants. Applicants have not addressed where the proteins are to be targeted, how to overcome deleterious growth effects due to overexpression a protein that is toxic to plant cells or how one optimizes expression levels of heterologous proteins or overcomes mechanisms of protein degradation inherent in all plant systems. Applicant has not shown the production levels recited in the claims.

Sharp et al (2001, *Biotechnology and Bioengineering* 73(5):338-346) teach overexpressing antibodies in plants produced fragments of the whole antibody that were the result of post-translational processing. Sharp et al reports "All of the molecules were actively secreted into the culture media and some showed evidence of Golgi-associated glycan processing, indicating they were not assembly intermediates" (abstract). Sharp et al conclude by stating "Identifying the nature of these degradative processes is a first step toward alleviating their effects, improving protein yields, and enhancing the feasibility of plants as a commercial means for large-scale protein production" (abstract).

Overexpressing heterologous proteins can cause unpredictable results. Elfstrand et al (2001, *Plant, Cell Reports* 20(7):596-603) reports the overexpression of peroxidase in Norway spruce "resulted in increased sensitivity to stress, leading to a reduction in epicotyl formation and in height growth compared with control plants" (abstract). Chaparro-Giraldo et al (2000, *Plant Cell Reports* 19(10) :961-965) reports that potato tubers transformed with a soybean leghemoglobin encoding nucleic acid reduced growth and decreased tuber production compared with untransformed plants. Chaparro-Giraldo et al concludes that targeting the leghemoglobin encoding nucleic acid to the chloroplast interfered with aerobic metabolism.

Applicant has not reduced to practice producing a wide range of protein amounts as specified in the application. Applicant is not just claiming amounts typically extracted in laboratories, but rather, Applicant is claiming a wide range of protein amounts ranging from 10 kilograms to over a ton (1000 kilograms) of protein/acre/year. This is an especially large amount given that the Applicants are growing these plants in an environmentally controlled facility. For the claims to be enabled, Applicants have to demonstrate that they can produce the quantities of protein that they are claiming.

Given the unpredictability of expressing a heterologous protein in a plant for the reasons stated above; and given the lack of guidance and examples of expressing any heterologous protein in a plant for the purpose of extracting or harvesting kilograms of said protein from plants grown under artificial conditions; given the state-of-the-art that teaches heterologous proteins are degraded due to post-translational processing and and heterologous proteins interfere with the normal development of plants, it would require undue experimentation by one skilled in the art to make and/or use the broadly claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 16-17 are rejected under 35 U.S.C. 102(b) as being anticipated by Rose et al (January, 1999, U.S. Patent 5,861,277).

The claims are drawn to a method of producing heterologous protein in a transformed plant comprising transforming a plant with an expression vector comprising a nucleic acid sequence encoding a heterologous protein operably linked to a promoter, growing the transformed plant in a plant growth facility in which the temperature and light are regulated, and extracting the heterologous protein, and wherein the plant is either a *Solanum*, *Spinacia* or *Brassica* species. For purposes of examination, the Office is interpreting the meaning of CEA as any plant growth facility in which the environmental conditions of the plant growth facility are regulated by any person.

Rose et al teach transforming a plant (columns 19-21), wherein the plant is a potato plant (column 6, line 42) with a heterologous nucleic acid encoding a protein (column 6, lines 11-67) and growing said transgenic plant under defined conditions (column 21, lines 25-41). Rose et al also disclose extracting proteins to verify expression levels of the heterologous proteins (column 9, figure 4. and column 28-29, Example 9) and as such anticipate the claimed invention.

5. Claims 29, 30, and 32 are rejected under 35 U.S.C. 102(b) as being anticipated by Thiele, et al (1999, Plant Physiology 120:73-81, listed in IDS).

Because of the 112 second issues which are discussed above, claim 29 is interpreted by the Office to encompass a method of making a transformed plant from which a heterologous protein is extracted, comprising transforming a plant that can be vegetatively propagated with a heterologous nucleic acid encoding a protein, and growing the plant in an artificial environment, and wherein the plant is potato.

Thiele et al teach potato plants transformed with a nucleic acid encoding a phytochrome protein (page 74, paragraph entitled "Plant Material") and growing the transformed plant in a controlled-environment chamber (page 74, paragraph entitled "Growth Conditions"). Thiele et al also teach a protein extract made from said plant (page 74, right column, 2nd paragraph) and as such Thiele et al anticipate the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

6. Claims 16-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rose et al (January, 1999, U.S. Patent 5,861,277) as applied to claims 16-17 above, and further in view of Fladung et al (1993 Plant Molecular Biology 23:749-757 listed in IDS) taken with Soper et al (July, 1999, U.S. Patent Number 5,920,002).

The claims are drawn to a method of producing heterologous protein in a transformed plant comprising transforming a plant with an expression vector comprising a nucleic acid sequence encoding a heterologous protein operably linked to a promoter, growing the transformed plant in a plant growth facility in which the temperature and light are regulated, and extracting the heterologous protein, and wherein the plant is either a *Solanum*, *Spinacia* or *Brassica* species and wherein the promoter is light-inducible and wherein the light-inducible

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promoter is from the Rubisco small subunit gene. For purposes of examination, the Office is interpreting the meaning of CEA as any plant growth facility in which the environmental conditions of the plant growth facility are regulated by any person.

The teachings of Rose et al have been discussed above.

Rose et al do not teach a light-inducible promoter or a light-inducible promoter from the small subunit of Rubisco.

Fladung et al teach the light-induced Rubisco small subunit promoter (page 750, right column, 1st paragraph).

Given the recognition of those of ordinary skill in the art of the value of producing a heterologous protein in a transformed plant that is grown in a controlled environment, one skilled in the art would have been motivated to transform a plant with a heterologous nucleic acid encoding a protein according to the method of Rose et al, and to incorporate a light-induced promoter such as the rubisco small subunit promoter as taught by Fladung et al for the purpose of increasing the rate of transcription in response to an inducing agent as disclosed by Soper et al (column 10, lines 47-48) and to generate the claimed invention with a reasonable expectation of success.

7. Claims 29-30, 32, and 34-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Thiele, et al (1999, Plant Physiology 120:73-81, listed in IDS) as applied to claims 29-30, and 32 above, and further in view of Fladung et al (1993 Plant Molecular Biology 23:749-757 listed in IDS) taken with Soper et al (July, 1999, U.S. Patent Number 5,920,002).

Because of the 112 second issues which are discussed above, claim 29 is interpreted by the Office to encompass a method of making a transformed plant from which a heterologous protein is extracted, comprising transforming a plant that can be vegetatively propagated and the protein can be extracted, with a heterologous nucleic acid encoding a protein, and growing the plant in an artificial environment, and wherein the plant is potato. Applicants further claim the above method in which the promoter is light-inducible and wherein the light-inducible promoter is the Rubisco small subunit promoter.

The teachings of Thiele et al have been discussed above.

Thiele et al do not teach a light-inducible promoter or a light-inducible promoter from the small subunit of Rubisco.

Fladung et al teach the light-induced Rubisco small subunit promoter (page 750, right column, 1st paragraph).

Given the recognition of those of ordinary skill in the art of the value of producing a heterologous protein in a transformed plant that is grown in a person-controlled environment, one skilled in the art would have been motivated to transform a plant that can be vegetatively propagated and the protein can be extracted with a heterologous nucleic acid encoding a protein according to the method of Thiele et al, and to incorporate a light-induced promoter such as the rubisco small subunit promoter as taught by Fladung et al for the purpose of increasing the rate of transcription in response to an inducing agent as disclosed by Soper et al (column 10, lines 47-48) and to generate the claimed invention with a reasonable expectation of success.

8. Claims 29-33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Thiele, et al (1999, Plant Physiology 120:73-81, listed in IDS) as applied to claims 29-30, and 32 above, and further in view of Dehesh et al (December, 1998, U.S. Patent Number 5,850,022).

Because of the 112 second issues which are discussed above, claim 29 is interpreted by the Office to encompass a method of making a transformed plant from which a heterologous protein is extracted, comprising transforming a plant that can be vegetatively propagated with a heterologous nucleic acid encoding a protein, and growing the plant in an artificial environment, and wherein the plant is potato and mustard.

The teachings of Thiele et al have been discussed above.

Thiele et al do not teach transforming a mustard plant

Dehesh et al teach transforming a *Brassica* plant which includes mustard plants (column 19, Example 4).

Given the recognition of those of ordinary skill in the art of the value of producing a heterologous protein in a transformed plant that is grown in a person-controlled environment, one skilled in the art would have been motivated to transform a plant that can be vegetatively propagated with a heterologous nucleic acid encoding a protein that can be easily extracted, according to the method of Thiele et al, and to modify this method for the transformation of *Brassica* as taught by Dehesh so as to grow a plant that grows well in an artificial environment and to generate the claimed invention with a reasonable expectation of success.

9. No claims are allowed.

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10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stuart Baum whose telephone number is (703) 305-6997. The examiner can normally be reached on Monday-Friday 8:30AM – 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (703) 306-3218. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3014 or (703) 305-3014 for regular communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the legal analyst, Tiffany Tabb, whose telephone number is (703) 605-1238.

Stuart F. Baum Ph.D.

December 31, 2002

Phuong Bui
PHUONG T. BUI
PRIMARY EXAMINER
1/13/03